STN- structure search 11/3/05

10/512,094

=> d ibib abs hitstr 1-57

L8 ANSWER 1 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:888946 CAPLUS
DOCUMENT NUMBER: 143:241958
TITLE: Methods for treating resistant or refractory tumors
INVENTOR(S): Caligiuri, Maureen; Wosikowski-Buters, Katja; Casazza, Anne Maria
PATENT ASSIGNEE(S): GPC Biotech AG, Germany
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005077385 | A2 | 20050825 | WO 2005-EP1733 | 20050218 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-546097P P 20040218

AB The instant invention relates to methods, pharmaceutical compns. and packaged pharmaceuticals for treating resistant or refractory tumors by administering platinum-based compds.

IT **215604-74-3**, BAY 38-3441
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for treating resistant or refractory tumors)

RN 215604-74-3 CAPLUS
CN L-Valine, N-[[[4-[(6-deoxy-3-O-methyl-β-L-galactopyranosyl)oxy]phenyl]amino]thioxomethyl]-L-histidyl-, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| US 2004037802 | A1 | 20040226 | US 2002-218167 | | 20020813 |
| CA 2493329 | AA | 20040219 | CA 2003-2493329 | | 20030813 |
| EP 1534334 | A1 | 20050601 | EP 2003-785231 | | 20030813 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | US 2002-218167 | A | 20020813 |
| | WO 2003-US25252 | W | 20030813 |

OTHER SOURCE(S): MARPAT 140:205131

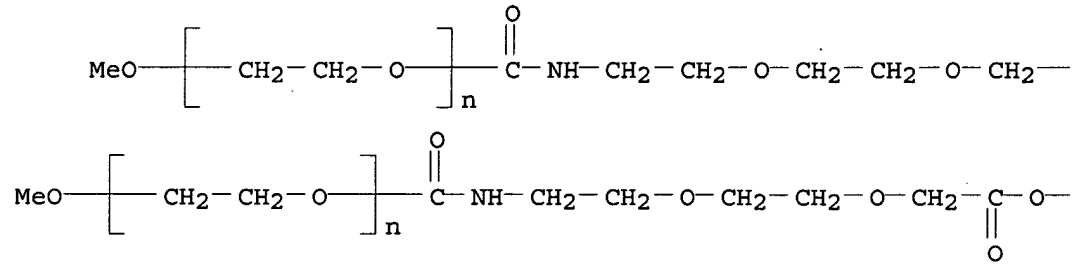
AB Activated polymeric bicine derivs. such as, as well as their conjugates are disclosed. Methods of making and using the bicine derivs. as prodrugs for treatment and diagnosis are also disclosed. For example, doxorubicin and daunorubicin prodrugs containing a polyethylene glycol derivative were prepared

IT **660843-26-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of polymeric conjugates based on aliphatic biodegradable linkers
as prodrugs)

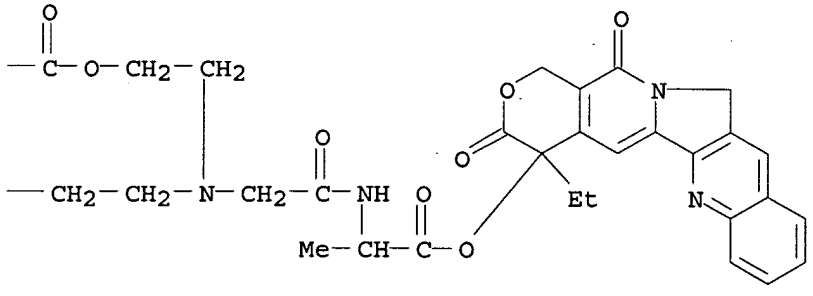
RN 660843-26-5 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-methoxy-, diester with N,N-bis[2-[[[2-[2-(carboxyamino)ethoxy]ethoxy]acetyl]oxy]ethyl]glycyl-L-alanine 2-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl] ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Inventor

L8 ANSWER 17 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN

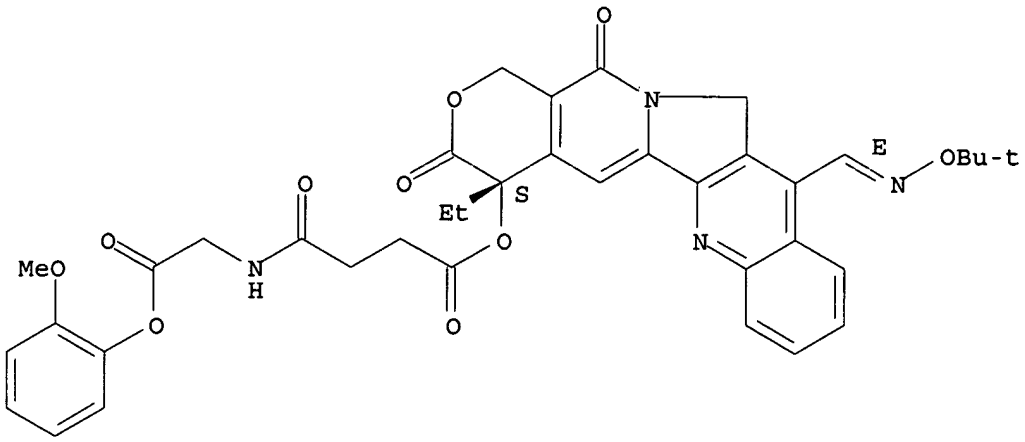
10/512,094

ACCESSION NUMBER: 2003:972082 CAPLUS
DOCUMENT NUMBER: 140:16851
TITLE: Preparation of esters in position 20 of camptothecins as antitumor agents
INVENTOR(S): Marzi, Mauro; Alloatti, Domenico; Pisano, Claudio; Tinti, Maria Ornella; Vesci, Loredana; Zunino, Franco
PATENT ASSIGNEE(S): Sigma-Tau Industrie Farmaceutiche Riunite S.p.A, Italy; Istituto Nazionale per lo Studio e la Cura dei Tumori
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003101996 | A2 | 20031211 | WO 2003-IT329 | 20030528 |
| WO 2003101996 | A3 | 20040129 | | |
| WO 2003101996 | C1 | 20040429 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2487252 | AA | 20031211 | CA 2003-2487252 | 20030528 |
| EP 1509529 | A2 | 20050302 | EP 2003-730481 | 20030528 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2005529935 | T2 | 20051006 | JP 2004-509687 | 20030528 |

PRIORITY APPLN. INFO.: IT 2002-RM306 A 20020531
WO 2003-IT329 W 20030528

OTHER SOURCE(S): MARPAT 140:16851
GI



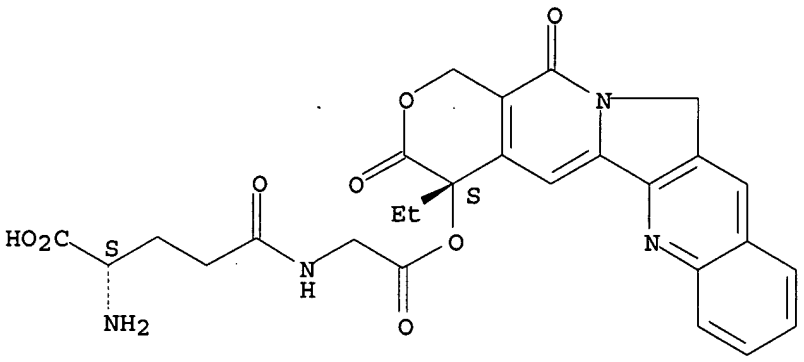
L8 ANSWER 18 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:811568 CAPLUS
DOCUMENT NUMBER: 141:111318
TITLE: Assessment of normal and tumor tissue uptake of MAG-CPT, a polymer-bound prodrug of camptothecin, in patients undergoing elective surgery for colorectal carcinoma
AUTHOR(S): Sarapa, Nenad; Britto, Margaret R.; Speed, William; Jannuzzo, MariaGabriella; Breda, Massimo; James, Christopher A.; Porro, Maria Grazia; Rocchetti, Maurizio; Wanders, Alkvin; Mahteme, Haile; Nygren, Peter
CORPORATE SOURCE: Department of Clinical Pharmacology, Pharmacia Corporation, Skokie, IL, 60077, USA
SOURCE: Cancer Chemotherapy and Pharmacology (2003), 52(5), 424-430
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB MAG-camptothecin (MAG-CPT) is the lead compound of a novel drug delivery system in which an active cytotoxic moiety, camptothecin (CPT), is covalently linked to a soluble polymeric carrier (MAG) to form an inactive prodrug. The mechanism of action of CPT remains unaltered, but the delivery system is thought to allow the carrier-bound drug to accumulate in tumor tissues and release the active CPT locally. This proof-of-concept clin. study was designed to determine whether MAG-CPT was preferentially delivered to or retained in tumor tissue compared to adjacent normal tissue or plasma, and to estimate the degree of intratissue release of CPT. MAG-bound and free CPT concns. in plasma, tumor, and normal tissue of patients achieved equilibrium by 24 h after dosing, declining in parallel up to 7 days after dosing. MAG-bound CPT was delivered to similar levels to tumor and normal tissue. At 24 h after dosing, the mean±SD MAG-bound CPT concns. were 861±216 ng/g in tumor and 751±215 ng/g in adjacent normal tissue, and free CPT concns. were lower in tumor than in normal tissue (12.2±4.7 ng/g and 21.9±6.7 ng/g, resp.). At 24 h after dosing, mean±SD ratios of MAG-bound and free CPT in tumor and plasma were 0.13±0.03 and 0.22±0.09, resp., and the ratios did not change for up to 7 days after dosing, indicating a lack of preferential retention of MAG-bound CPT or release of free CPT in tumor. These results are in marked contrast to previous data from animal tumor xenograft studies, where MAG-CPT levels were higher in tissue than in plasma at 3 and 7 days after a single i.v. dose. Delivery of CPT to the

CM 1

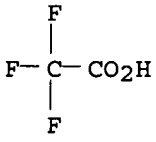
CRN 476651-89-5
CMF C27 H26 N4 O8

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L8 ANSWER 24 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:917633 CAPLUS
DOCUMENT NUMBER: 138:117380
TITLE: Synthesis and in Vivo Antitumor Activity of Poly(L-glutamic acid) Conjugates of 20(S)-Camptothecin
AUTHOR(S): Bhatt, Rama; de Vries, Peter; Tulinsky, John; Bellamy, Garland; Baker, Brian; Singer, Jack W.; Klein, Peter
CORPORATE SOURCE: Cell Therapeutics, Inc., Seattle, WA, 98119, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(1), 190-193
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

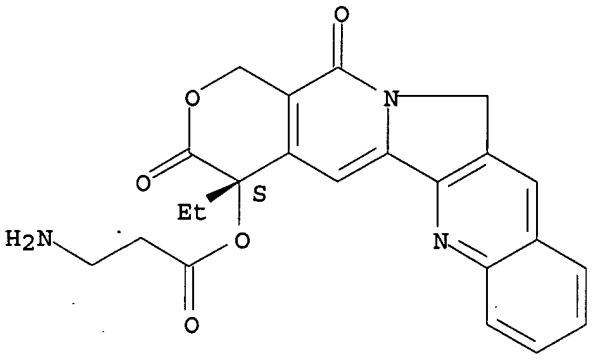
AB Poly-α-(L-glutamic acid) (PG) conjugates of 20(S)-camptothecin (CPT) displayed improved aqueous solubility compared to CPT, were stable in aqueous solution at neutral pH, and were potent antitumor agents in vivo. Evaluation of PG mol. weight, CPT loading, aqueous solubility, and CPT equivalent dosing with respect to in vivo antitumor potencies of various linked conjugates led to identification of a preferred conjugate composition

IT **182691-89-0DP**, conjugate with poly(L-glutamic acid)
**362496-92-2DP**, conjugate with poly(L-glutamic acid)
**362496-97-7DP**, conjugate with poly(L-glutamic acid)
**362497-02-7DP**, conjugate with poly(L-glutamic acid)
**362497-07-2DP**, conjugate with poly(L-glutamic acid)

**476654-49-6DP**, conjugate with poly(L-glutamic acid)
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and in vivo antitumor activity of poly(L-glutamic acid) conjugates of 20(S)-camptothecin)

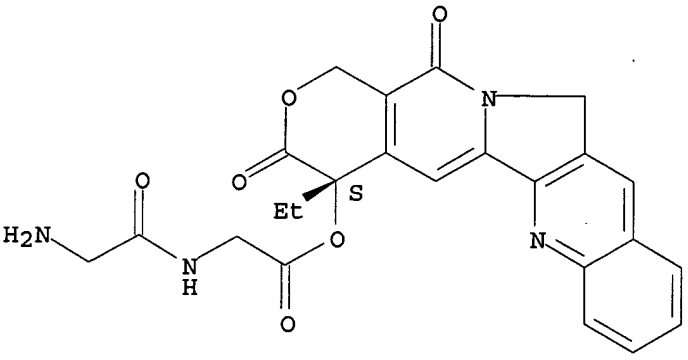
RN 182691-89-0 CAPLUS
CN β-Alanine, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



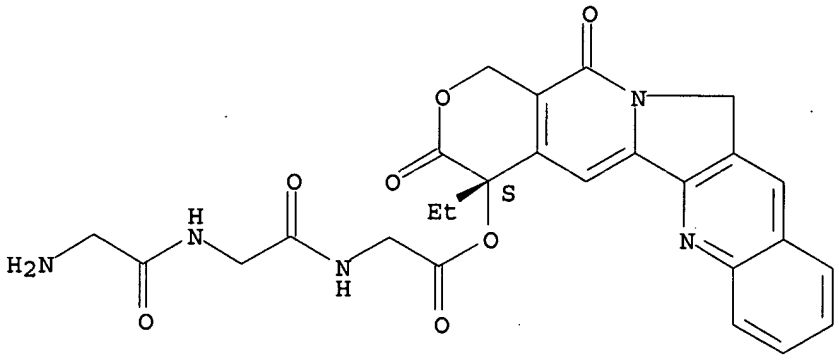
RN 362496-92-2 CAPLUS
CN Glycine, glycyl-, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



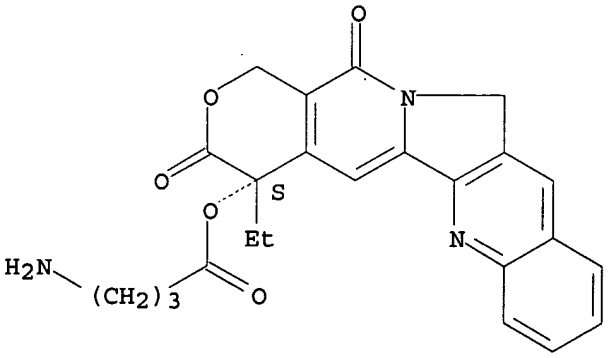
RN 362496-97-7 CAPLUS
CN Glycine, glycylglycyl-, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



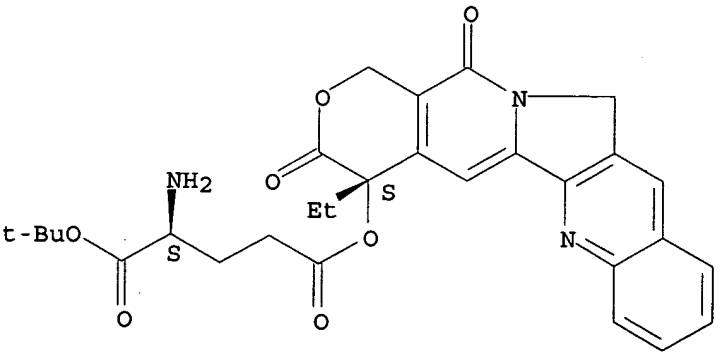
RN 362497-02-7 CAPLUS
CN Butanoic acid, 4-amino-, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

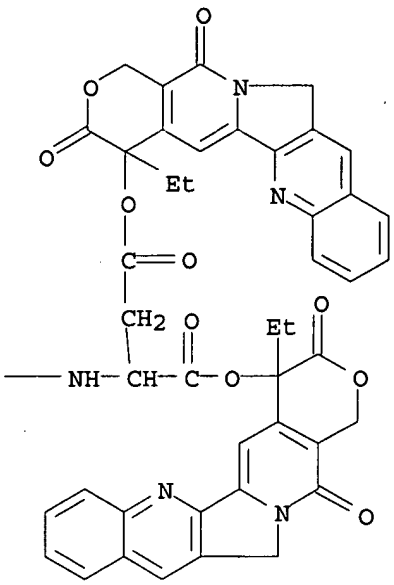


RN 362497-07-2 CAPLUS
CN L-Glutamic acid, 1-(1,1-dimethylethyl) 5-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 476654-49-6 CAPLUS
CN L-Glutamic acid, 5-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl] ester (9CI) (CA INDEX



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 32 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:777238 CAPLUS
DOCUMENT NUMBER: 136:79270
TITLE: Design and Optimization of 20-O-Linked Camptothecin Glycoconjugates as Anticancer Agents
AUTHOR(S): Lerchen, Hans-Georg; Baumgarten, Joerg; von Bruch, Karsten; Lehmann, Thomas E.; Sperzel, Michael; Kempka, Grazyna; Fiebig, Heinz-Herbert
CORPORATE SOURCE: Central Research Life Sciences, Bayer AG, Leverkusen, 51368, Germany
SOURCE: Journal of Medicinal Chemistry (2001), 44(24), 4186-4195
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:79270

AB To improve the biol. profile of 20(S)-camptothecin, a novel class of 20-O-linked camptothecin glycoconjugates has been designed for preferential cellular uptake into tumor cells by an active transport mechanism. Such conjugates have been optimized for enhanced solubility, stabilization of the camptothecin lactone ring, sufficient hydrolytic and proteolytic stability, and for an overall improvement in tumor selectivity. The constitution of the peptide spacer has a major impact on stability and biol. activity of the conjugates both in vitro and in vivo. Some of Glycoconjugates with valine residues at the linkage position to camptothecin are sufficiently stable and show good antitumor activity in vitro against HT29 and other tumor cell lines. Fluorescence microscopy and flow cytometry expts. indicate that glycoconjugates are taken up into lysosomal compartments of the tumor cell line HT29 by an active transport mechanism. The steric configuration of the particular amino acid residues linked to the camptothecin moiety has a major impact on the in vivo activity of the corresponding glycoconjugates in the breast cancer xenograft MX-1 model. Inhibiting tumor growth by >96%, glycoconjugates show the best activity in this particular model and have been investigated

more extensively. One of the glycoconjugates compares favorably to topotecan and other glycoconjugate with respect to toxicity against hematopoietic stem cells and hepatocytes. Based on its profile, glycoconjugate (BAY 38-3441) has been selected for clin. trials.

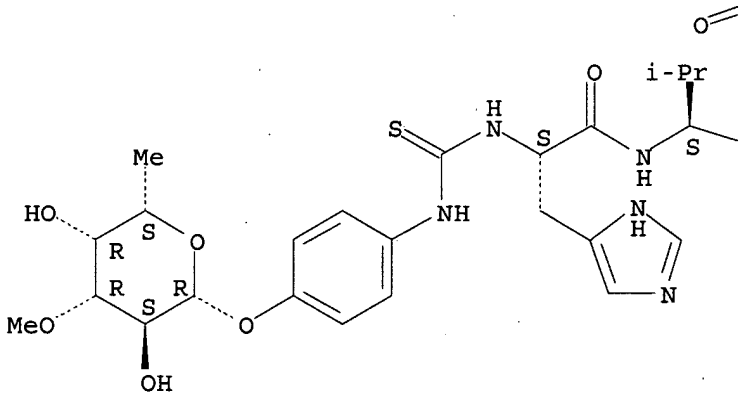
IT **215604-74-3P**, BAY 38-3441
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(design and optimization of 20-O-linked camptothecin glycoconjugates as anticancer agents)

RN 215604-74-3 CAPLUS

CN L-Valine, N-[[[4-[(6-deoxy-3-O-methyl-β-L-galactopyranosyl)oxy]phenyl]amino]thioxomethyl]-L-histidyl-, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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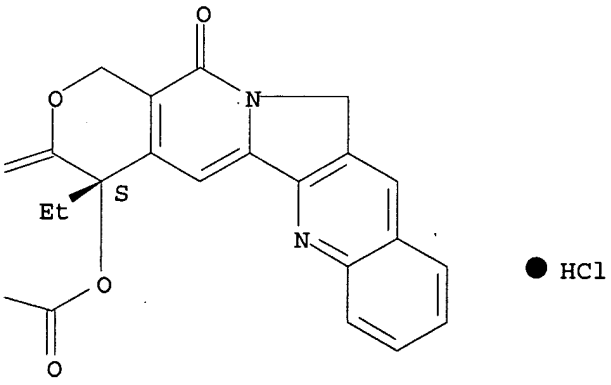

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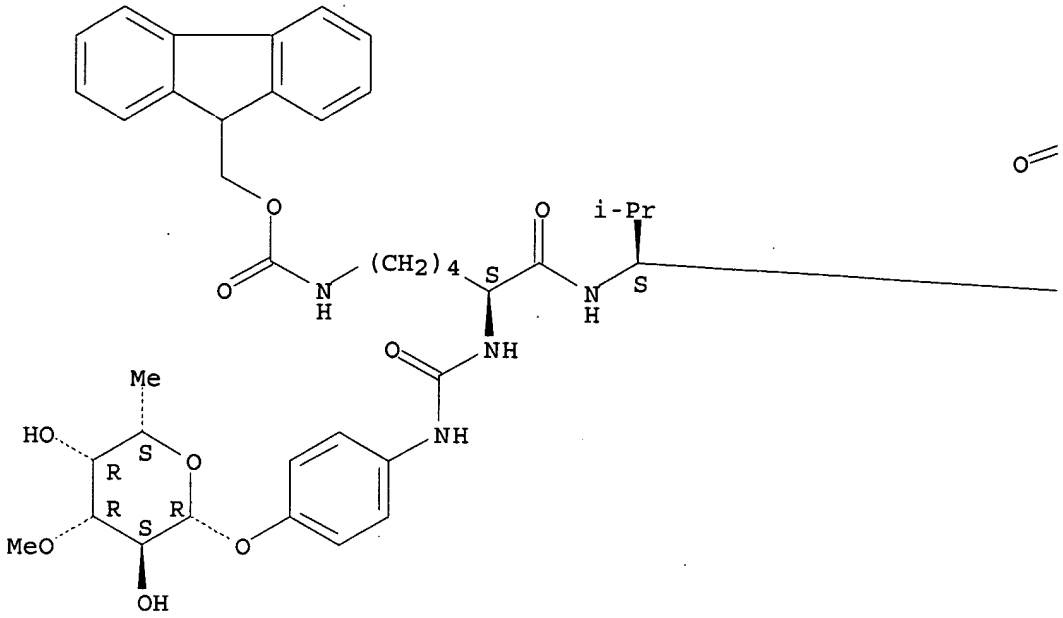

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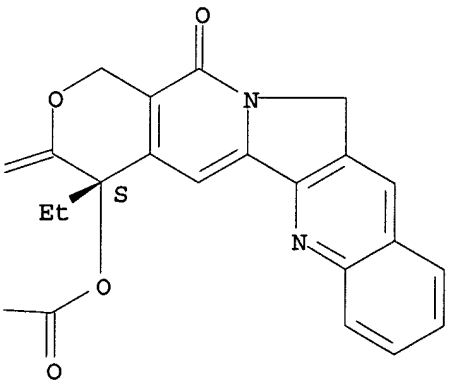

L8 ANSWER 37 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:507704 CAPLUS
DOCUMENT NUMBER: 135:77105
TITLE: Preparation of camptothecin β-alanine esters having topoisomerase I inhibitory activity
INVENTOR(S): Wall, Monroe E.; Wani, Mansukh C.; Manikumar, Govindarajan; Balasubramanian, Neelakantan; Vyas, Dolatrai
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001049691 | A1 | 20010712 | WO 2000-US15033 | 20000614 |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6288072 | B1 | 20010911 | US 1999-474099 | 19991229 |
| CA 2396030 | AA | 20010712 | CA 2000-2396030 | 20000614 |
| EP 1254141 | A1 | 20021106 | EP 2000-939454 | 20000614 |
| EP 1254141 | B1 | 20050817 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003519234 | T2 | 20030617 | JP 2001-550231 | 20000614 |
| AT 302204 | E | 20050915 | AT 2000-939454 | 20000614 |
| NO 2002003175 | A | 20020829 | NO 2002-3175 | 20020628 |
| PRIORITY APPLN. INFO.: | | | US 1999-474099 A | 19991229 |
| | | | WO 2000-US15033 W | 20000614 |

OTHER SOURCE(S): MARPAT 135:77105

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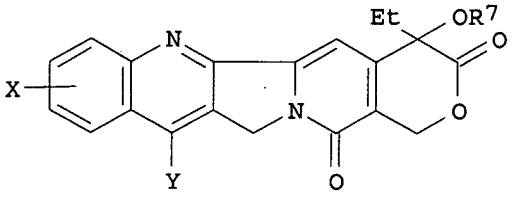


I

AB Camptothecin β-alanine esters I [X and Y are each independently NO2, NH2, H, F, Cl, Br, I, CO2H, OH, O-C1-6 alkyl, SH, S-C1-6 alkyl, CN, NH-C1-6 alkyl, N(C1-6 alkyl)2, CHO, C1-8 alkyl, N3, -Z(CH2)aN[(CH2)bOH]2 or -Z(CH2)aN(C1-6 alkyl)2, where Z is O, NH, S and a and b are 2 or 3, -CH2-L, where L is halo, N2+, OSO2CF3, acyl, alkyl- or arylsulfonyl, dialkylamino, etc.; R7 is COCH2CH2NR8R9 (R8, R9 = H, C1-6 alkyl), CO(CH2)mNR10R11 or COCHR12NR13R14, where m = 1 or 2, R12 is the side chain of a naturally occurring α-amino acid and R10, R11, R13 and R14 are H or C1-8 alkyl] and 3-X-substituted 4,5-(methylenedioxy)- or 4,5-(ethylenedioxy)benzo derivs. were prepared for use as antitumor agents. These compds. inhibit the enzyme topoisomerase I and may alkylate DNA of the associated topoisomerase I-DNA cleavable complex. Thus, 10,11-methylenedioxycamptothecin-20-β-Ala-Lys ester dihydrochloride was prepared by esterification of 10,11-methylenedioxy-20(S)-camptothecin with Boc-Lys(BOC)-β-Ala-OH (Boc = tert-butoxycarbonyl), followed by Boc-deprotection with HCl-saturated dioxane.

IT **182691-89-0P 347417-50-9P**

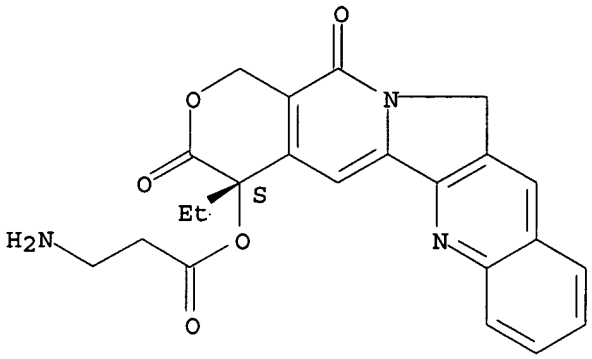
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of camptothecin β-alanine esters having topoisomerase I inhibitory activity)

RN 182691-89-0 CAPLUS

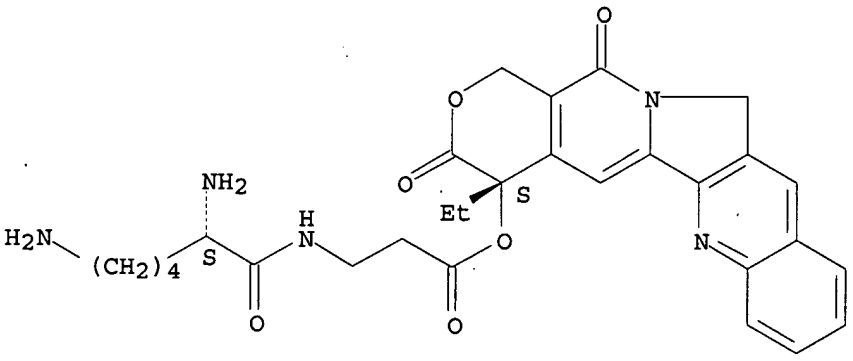
CN β-Alanine, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 347417-50-9 CAPLUS
CN β-Alanine, L-lysyl-, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



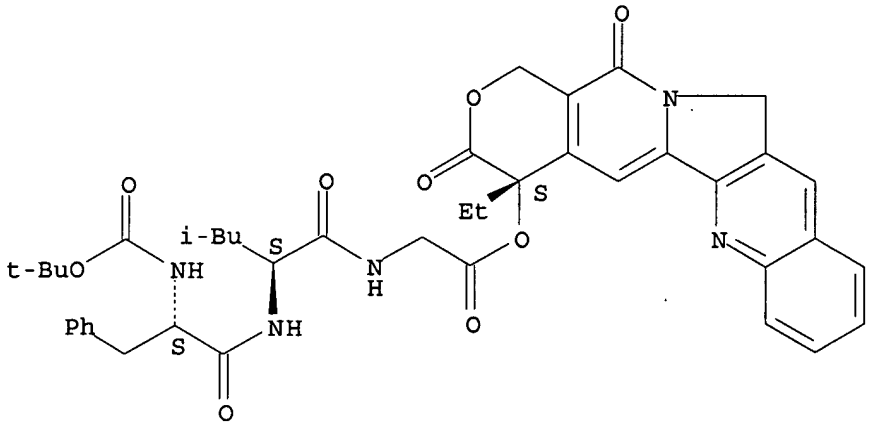
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 38 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:468173 CAPLUS
DOCUMENT NUMBER: 135:66230
TITLE: Biodegradable high molecular weight polymeric linkers and their conjugates
INVENTOR(S): Greenwald, Richard B.; Martinez, Anthony J.; Choe, Yun H.; Pendri, Annapurna
PATENT ASSIGNEE(S): Enzon, Inc., USA
SOURCE: U.S., 32 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-L-leucyl-, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 47 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:690979 CAPLUS
DOCUMENT NUMBER: 131:322821
TITLE: Preparation of terminally-branched polymeric linkers and polymeric conjugates containing them as pro drugs.
INVENTOR(S): Martinez, Anthony J.; Pendri, Annapurna; Greenwald, Richard B.; Choe, Yun H.
PATENT ASSIGNEE(S): Enzon, Inc., USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9953951 | A1 | 19991028 | WO 1999-US8373 | 19990416 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6153655 | A | 20001128 | US 1998-62305 | 19980417 |
| CA 2328922 | AA | 19991028 | CA 1999-2328922 | 19990416 |
| AU 9936483 | A1 | 19991108 | AU 1999-36483 | 19990416 |
| EP 1071455 | A1 | 20010131 | EP 1999-918611 | 19990416 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002512265 | T2 | 20020423 | JP 2000-544354 | 19990416 |

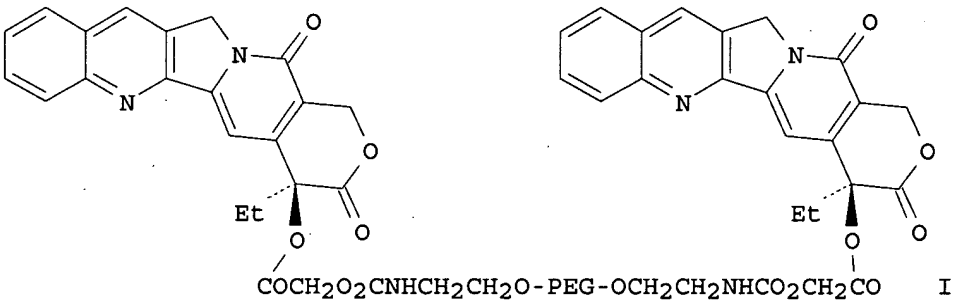
PRIORITY APPLN. INFO.:
US 1998-62305 A 19980417
WO 1999-US8373 W 19990416

L8 ANSWER 48 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:655948 CAPLUS
DOCUMENT NUMBER: 131:286688
TITLE: Preparation of high molecular weight polymer-based prodrugs
INVENTOR(S): Greenwald, Richard B.; Pendri, Annapurna; Zhao, Hong
PATENT ASSIGNEE(S): Enzon, Inc., USA
SOURCE: U.S., 39 pp., Cont.-in-part of U.S. 5,840,900.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5965566 | A | 19991012 | US 1997-914927 | 19970820 |
| US 5614549 | A | 19970325 | US 1995-380873 | 19950130 |
| US 5880131 | A | 19990309 | US 1995-537207 | 19950929 |
| US 5840900 | A | 19981124 | US 1996-700269 | 19960820 |
| US 6127355 | A | 20001003 | US 1999-277230 | 19990326 |

PRIORITY APPLN. INFO.:
US 1993-140346 B2 19931020
US 1995-380873 A2 19950130
US 1995-537207 A2 19950929
US 1996-700269 A2 19960820
US 1992-934131 B2 19920821
US 1993-28743 B2 19930309
US 1997-914927 A1 19970820

GI




I

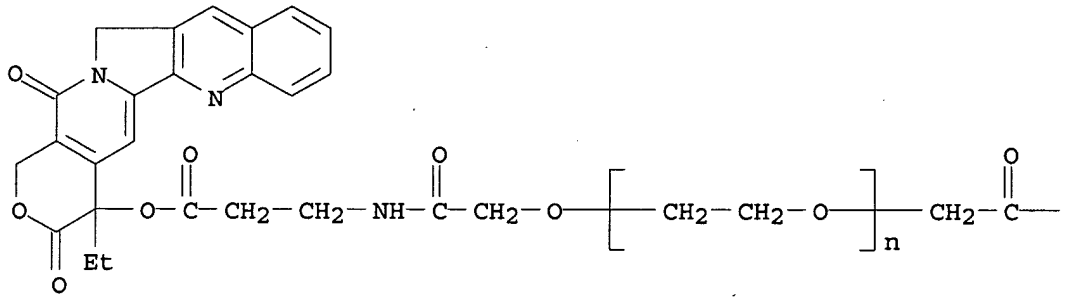
AB Compns. of formula DY1C(:Y)(CR1R2)nXR3 [D = biol. active moiety, e.g. camptothecin, paclitaxel, podophyllotoxin; Y, Y1 = O, S; R1, R2 = H, alkyl, aryl, heteroalkyl, etc.; n = 0-12; X = electron withdrawing group; R3 = non-antigenic polymer, e.g. polyethylene glycol (PEG) having a mol. weight of at least about 20,000, alkyl, cycloalkyl, acyl, carboalkoxy alkyl, dialkylaminoalkyl, phenylalkyl, phenylaryl] are prepared as water soluble prodrugs. Thus, I was prepared from camptothecin, benzyloxyacetic acid and PEG(40k) bis(2-isocyanatoethyl) ether. I showed antileukemic (IC50 = 7 nM vs. P388) and antitumor activity (IC50 = 30 nM vs. HT-29).

IT **204133-45-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of water soluble polymer-based prodrugs from natural products)

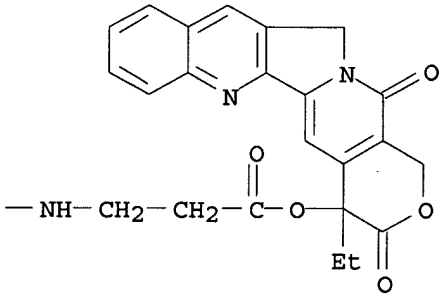
RN 204133-45-9 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[3-[[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-

yl]oxy]-3-oxopropyl]amino]-2-oxoethyl]-ω-[2-[[3-[[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl]oxy]-3-oxopropyl]amino]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 49 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:461752 CAPLUS
DOCUMENT NUMBER: 131:276856
TITLE: Multiple event activation of a generic prodrug trigger by antibody catalysis
AUTHOR(S): Shabat, Doron; Rader, Christoph; List, Benjamin; Lerner, Richard A.; Barbas, Carlos F., III
CORPORATE SOURCE: The Skaggs Institute for Chemical Biology and the Department of Molecular Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(12), 6925-6930
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

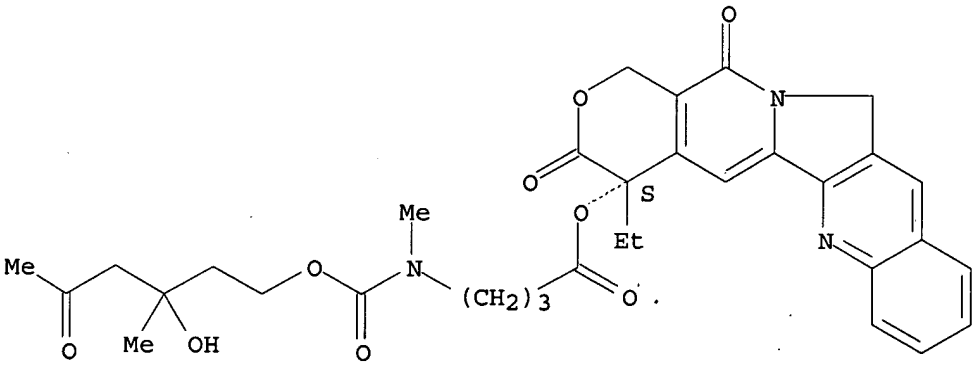
AB Chemotherapeutic regimes are typically limited by nonspecific toxicity. To address this problem we have developed a broadly applicable drug-masking chemical that operates in conjunction with a unique broad-scope catalytic antibody. This masking chemical is applicable to a wide range of drugs because it is compatible with virtually any heteroatom. We demonstrate that generic drug-masking groups may be selectively removed by sequential retro-aldolretro-Michael reactions catalyzed by antibody 38C2. This reaction cascade is not catalyzed by any known natural enzyme. Application of this masking chemical to the anticancer drugs doxorubicin and

camptothecin produced prodrugs with substantially reduced toxicity. These prodrugs are selectively unmasked by the catalytic antibody when it is applied at therapeutically relevant concns. We have demonstrated the efficacy of this approach by using human colon and prostate cancer cell lines. The antibody demonstrated a long in vivo half-life after administration to mice. Based on these findings, we believe that the system described here has the potential to become a key tool in selective chemotherapeutic strategies.

IT **245330-19-2P 245330-20-5P**
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(multiple event activation of a generic prodrug trigger by antibody catalysis)

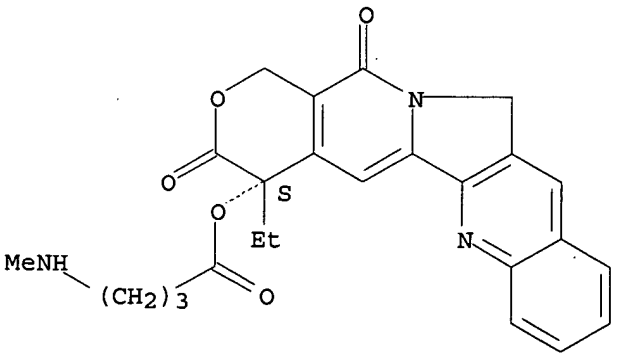
RN 245330-19-2 CAPLUS
CN Butanoic acid, 4-[[[(3-hydroxy-3-methyl-5-oxohexyl)oxy]carbonyl]methylamino]-, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 245330-20-5 CAPLUS
CN Butanoic acid, 4-(methylamino)-, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

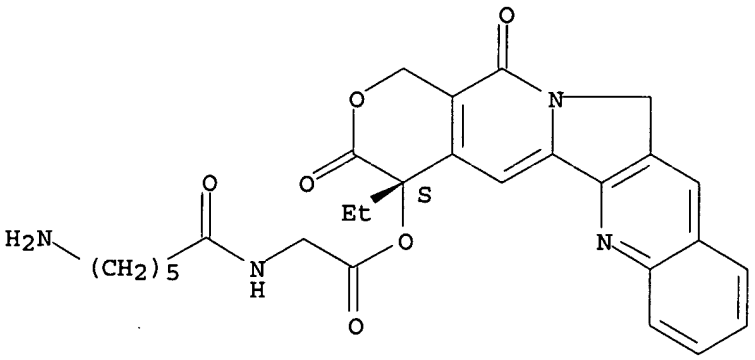
ACCESSION NUMBER: 1999:249104 CAPLUS
DOCUMENT NUMBER: 130:276739
TITLE: Preparation of polymeric derivatives of camptothecins having antitumor activity
INVENTOR(S): Angelucci, Francesco; Orzi, Fabrizio; Fachin, Gabriele; Caiolfa, Valeria; Zamai, Moreno; Suarato, Antonino
PATENT ASSIGNEE(S): Pharmacia & Upjohn S.P.A., Italy
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9917804 | A1 | 19990415 | WO 1998-EP6048 | 19980922 |
| W: AU, BG, BR, CA, CN, CZ, HR, HU, IL, JP, KR, MX, NO, NZ, PL, RO, SG, SI, UA, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| TW 564178 | B | 20031201 | TW 1998-87115168 | 19980911 |
| CA 2303097 | AA | 19990415 | CA 1998-2303097 | 19980922 |
| AU 9896273 | A1 | 19990427 | AU 1998-96273 | 19980922 |
| AU 749321 | B2 | 20020620 | | |
| EP 1019090 | A1 | 20000719 | EP 1998-950071 | 19980922 |
| EP 1019090 | B1 | 20040218 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2001518521 | T2 | 20011016 | JP 2000-514673 | 19980922 |
| NZ 503879 | A | 20020328 | NZ 1998-503879 | 19980922 |
| BR 9815236 | A | 20020723 | BR 1998-15236 | 19980922 |
| AT 259662 | E | 20040315 | AT 1998-950071 | 19980922 |
| PT 1019090 | T | 20040531 | PT 1998-950071 | 19980922 |
| ES 2216317 | T3 | 20041016 | ES 1998-950071 | 19980922 |
| ZA 9808923 | A | 19990412 | ZA 1998-8923 | 19980930 |
| MX 200003031 | A | 20001110 | MX 2000-3031 | 20000328 |
| NO 2000001628 | A | 20000329 | NO 2000-1628 | 20000329 |
| US 6328953 | B1 | 20011211 | US 2000-509534 | 20000331 |
| BG 104355 | A | 20010131 | BG 2000-104355 | 20000419 |
| HK 1032005 | A1 | 20050401 | HK 2001-102639 | 20010412 |

PRIORITY APPLN. INFO.: GB 1997-21069 A 19971003
WO 1998-EP6048 W 19980922

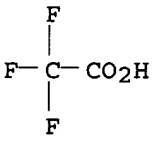
AB Water soluble polymeric conjugates of camptothecin comprise N-(2-hydroxypropyl)methacryloylamide units linked via a spacer of the formula -Gly-(CH2)n-CO-Gly (n = 2-8 to the C-20 position of a camptothecin residue). The conjugates possess enhanced antitumor activity and decreased toxicity with respect to the free drug. A process for their preparation and pharmaceutical compns. containing them are also described. Thus, 20-O-[methacryloyl-glycyl-(6-aminohexanoyl)-glycyl]camptothecin 1.26, N-(2-hydroxypropyl)methacrylamide 4.4, and 2,2'-azobisisobutyronitrile 0.26 g were dissolved with anhydrous dimethylsulfoxide, kept 60° under nitrogen and stirred for 24 h. The reaction mixture was then cooled at room temp and poured into Et acetate to obtain a precipitate which was collected, washed, re-precipitated, and dried to obtain MAG-camptothecin (I). I was tested on human colon carcinoma transplanted in nude mice. I was non-toxic and gave 95% tumor inhibition at all tested doses (15-22.5 mg/kg) with an exceptional high number of tumor-free animals after 90 days.

IT **246527-99-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 51 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:774306 CAPLUS
DOCUMENT NUMBER: 130:20601
TITLE: High molecular weight polymer-based prodrugs
INVENTOR(S): Greenwald, Richard B.; Pendri, Annapurna
PATENT ASSIGNEE(S): Enzon Inc., USA
SOURCE: U.S., 33 pp., Cont.-in-part of U.S. Ser. No. 537,207.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5840900 | A | 19981124 | US 1996-700269 | 19960820 |
| US 5614549 | A | 19970325 | US 1995-380873 | 19950130 |
| US 5880131 | A | 19990309 | US 1995-537207 | 19950929 |
| CA 2263409 | AA | 19980226 | CA 1997-2263409 | 19970820 |
| WO 9807713 | A1 | 19980226 | WO 1997-US14692 | 19970820 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9740794 | A1 | 19980306 | AU 1997-40794 | 19970820 |
| AU 730244 | B2 | 20010301 | | |

| | | | | |
|---|---|---|---|---|
| EP 923566 | A1 | 19990623 | EP 1997-938484 | 19970820 |
| EP 923566 | B1 | 20031029 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| US 5965566 | A | 19991012 | US 1997-914927 | 19970820 |
| NZ 334283 | A | 20000327 | NZ 1997-334283 | 19970820 |
| JP 2000517304 | T2 | 20001226 | JP 1998-510949 | 19970820 |
| AT 253060 | E | 20031115 | AT 1997-938484 | 19970820 |
| PT 923566 | T | 20040331 | PT 1997-938484 | 19970820 |
| ES 2210564 | T3 | 20040701 | ES 1997-938484 | 19970820 |
| US 6127355 | A | 20001003 | US 1999-277230 | 19990326 |
| PRIORITY APPLN. INFO.: | | | US 1993-140346 | B2 19931020 |
| | | | US 1995-380873 | A2 19950130 |
| | | | US 1995-537207 | A2 19950929 |
| | | | US 1992-934131 | B2 19920821 |
| | | | US 1993-28743 | B2 19930309 |
| | | | US 1996-700269 | A 19960820 |
| | | | US 1997-914927 | A1 19970820 |
| | | | WO 1997-US14692 | W 19970820 |

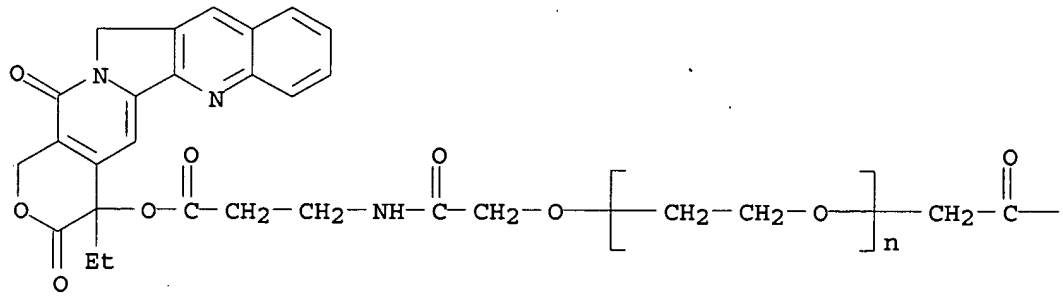

AB The present invention concerns polymeric prodrugs, DY'C(:Y)(CH2)nR1XR2, (where D is a biol. active moiety; X is an electron withdrawing group; Y and Y' are independently O or S; R1 = H, C1-6 alkyl, aryl, substituted aryl, aralkyl, heteroalkyl, n = 1-12; and R2 is a polyalkylene oxide). In preferred embodiments, the prodrugs contain a polyethylene glycol having a mol. weight of at least about 20,000. Thus, camptothecin 20-O ester of benzyloxyacetic acid was prepd.and hydrogenolyzed, and the resulting product was treated with N,N-carbonyldiimidazole and PEG diisocyanate. The antileukemia activity of some of the prodrugs was demonstrated.

IT **204133-45-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of high mol. weight polymer-based prodrugs)

RN 204133-45-9 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[2-[[3-[[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl]oxy]-3-oxopropyl]amino]-2-oxoethyl]-ω-[2-[[3-[[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl]oxy]-3-oxopropyl]amino]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



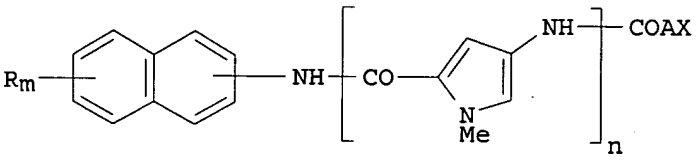
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 56 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:656434 CAPLUS
DOCUMENT NUMBER: 125:300690
TITLE: Preparation of conjugates of biologically active compounds with polypyrrolecarboxamidonaphthalene derivatives with increased bioavailability.
INVENTOR(S): Mongelli, Nicola; Biasoli, Giovanni; Lombardi Borgia, Andrea; Ciomei, Marina; Pesenti, Enrico; Angelucci, Francesco
PATENT ASSIGNEE(S): Pharmacia S.P.A., Italy
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9626950 | A1 | 19960906 | WO 1996-EP528 | 19960208 |
| W: AM, AU, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN, AZ, BY, KG, KZ, RU | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2189358 | AA | 19960906 | CA 1996-2189358 | 19960208 |
| AU 9648698 | A1 | 19960918 | AU 1996-48698 | 19960208 |
| AU 696470 | B2 | 19980910 | | |
| EP 758339 | A1 | 19970219 | EP 1996-904024 | 19960208 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE | | | | |
| CN 1148391 | A | 19970423 | CN 1996-190152 | 19960208 |
| JP 10504319 | T2 | 19980428 | JP 1996-525980 | 19960208 |
| ZA 9601636 | A | 19960906 | ZA 1996-1636 | 19960229 |
| FI 9604331 | A | 19961101 | FI 1996-4331 | 19961028 |
| NO 9604610 | A | 19961031 | NO 1996-4610 | 19961031 |

PRIORITY APPLN. INFO.: GB 1995-4065 A 19950301
WO 1996-EP528 W 19960208

OTHER SOURCE(S): MARPAT 125:300690
GI

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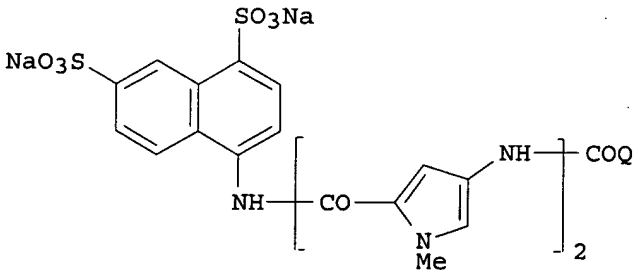


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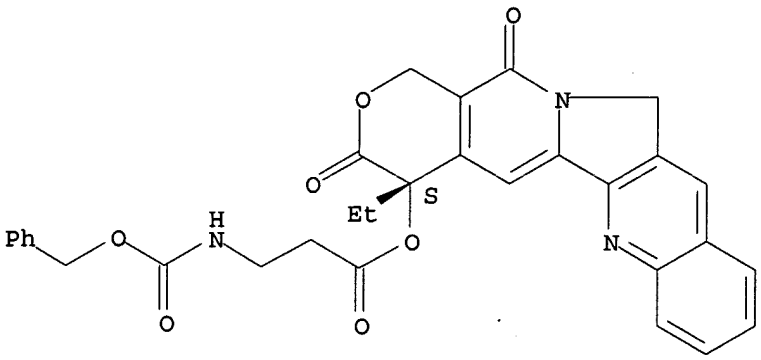
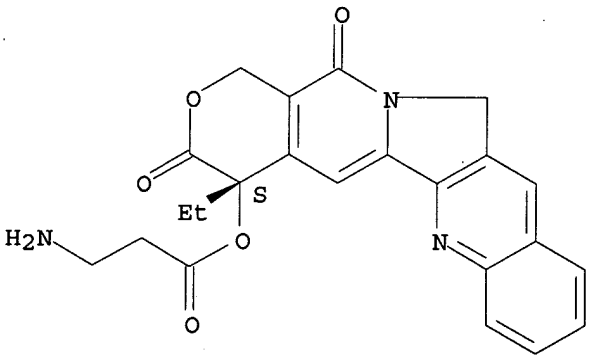


RN 182691-90-3 CAPLUS
CN β-Alanine, 4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester, (S)-, monoformate (9CI) (CA INDEX NAME)

CM 1

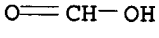
CRN 182691-89-0
CMF C23 H21 N3 O5

Absolute stereochemistry.



CM 2

CRN 64-18-6
CMF C H2 O2



L8 ANSWER 57 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:665139 CAPLUS
DOCUMENT NUMBER: 123:65831
TITLE: Polymer-bound camptothecin derivatives
INVENTOR(S): Angelucci, Francesco; Suarato, Antonino
PATENT ASSIGNEE(S): Pharmacia S.P.A., Italy
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 9510304 | A1 | 19950420 | WO 1994-EP3154 | | 19940921 |
| W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, US, UZ, VN | | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | | |
| CA 2150132 | AA | 19950420 | CA 1994-2150132 | | 19940921 |
| AU 9477836 | A1 | 19950504 | AU 1994-77836 | | 19940921 |
| AU 679788 | B2 | 19970710 | | | |
| EP 673258 | A1 | 19950927 | EP 1994-928387 | | 19940921 |
| EP 673258 | B1 | 20030507 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE | | | | | |
| CN 1115564 | A | 19960124 | CN 1994-190775 | | 19940921 |
| HU 71678 | A2 | 19960129 | HU 1995-2084 | | 19940921 |
| HU 215588 | B | 19990128 | | | |
| JP 08504217 | T2 | 19960507 | JP 1995-511221 | | 19940921 |
| PL 178132 | B1 | 20000331 | PL 1994-309328 | | 19940921 |
| RU 2149646 | C1 | 20000527 | RU 1995-112841 | | 19940921 |
| AT 239507 | E | 20030515 | AT 1994-928387 | | 19940921 |
| PT 673258 | T | 20030930 | PT 1994-928387 | | 19940921 |
| ES 2198421 | T3 | 20040201 | ES 1994-928387 | | 19940921 |
| IL 111173 | A1 | 19981030 | IL 1994-111173 | | 19941005 |
| ZA 9407823 | A | 19950703 | ZA 1994-7823 | | 19941006 |
| FI 9502746 | A | 19950605 | FI 1995-2746 | | 19950605 |
| US 5773522 | A | 19980630 | US 1995-448330 | | 19950608 |
| PRIORITY APPLN. INFO.: | | | GB 1993-20781 | A | 19931008 |
| | | | WO 1994-EP3154 | W | 19940921 |

AB A water-soluble polymeric conjugates with antitumor activity consist of (i) 60-99 mol% N-(2-hydroxypropyl)methacryloylamide units, (ii) 1-40 mol% 20-O-(N-methacryloylglycylaminoacyl)camptothecin units, and (iii) 0-10 mol% N-methacryloylglycine or N-(2-hydroxypropyl)methacryloylglycinamide units. Copolymer of N-(2-hydroxypropyl)methacryloylamide, 20-O-[N-methacryloylglycyl-(6-aminohexanoyl)]camptothecin, and N-(2-hydroxypropyl)methacryloylglycinamide was prepared and released 10% camptothecin after 120 h.

IT **164725-90-0P 164725-92-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antitumor camptothecin polymer conjugates)

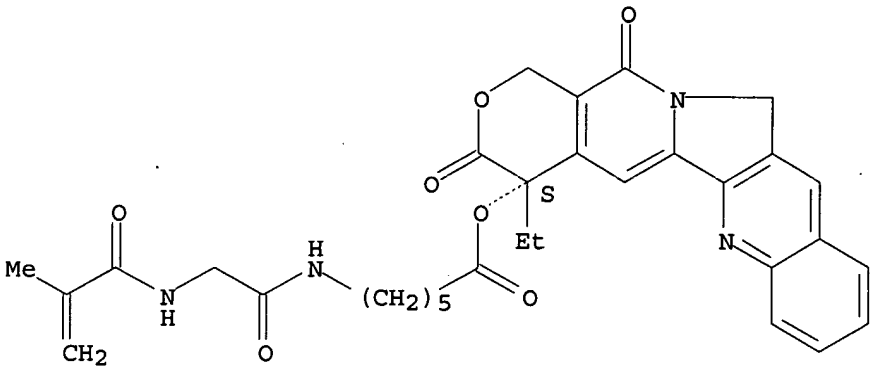
RN 164725-90-0 CAPLUS

CN Hexanoic acid, 6-[[[(2-methyl-1-oxo-2-propenyl)amino]acetyl]amino]-, 4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester, (S)-, polymer with N-[2-[(2-hydroxypropyl)amino]-2-oxoethyl]-2-methyl-2-propenamide and N-(2-hydroxypropyl)-2-methyl-2-propenamide (9CI) (CA INDEX NAME)

CM 1

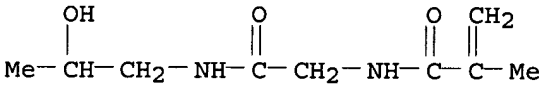
CRN 164725-89-7
CMF C32 H34 N4 O7

Absolute stereochemistry.



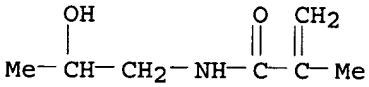
CM 2

CRN 153986-34-6
CMF C9 H16 N2 O3



CM 3

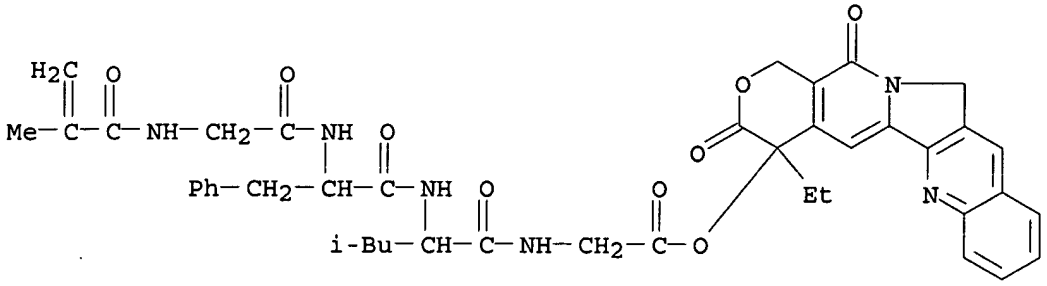
CRN 21442-01-3
CMF C7 H13 N O2



RN 164725-92-2 CAPLUS
CN Glycine, N-[N-[N-[N-(2-methyl-1-oxo-2-propenyl)glycyl]-L-phenylalanyl]-L-leucyl]-, 4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester, (S)-, polymer with N-[2-[(2-hydroxypropyl)amino]-2-oxoethyl]-2-methyl-2-propenamide and N-(2-hydroxypropyl)-2-methyl-2-propenamide (9CI) (CA INDEX NAME)

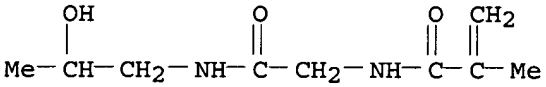
CM 1

CRN 164725-91-1
CMF C43 H46 N6 O9



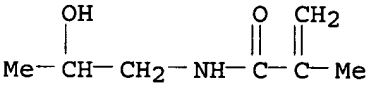
CM 2

CRN 153986-34-6
CMF C9 H16 N2 O3



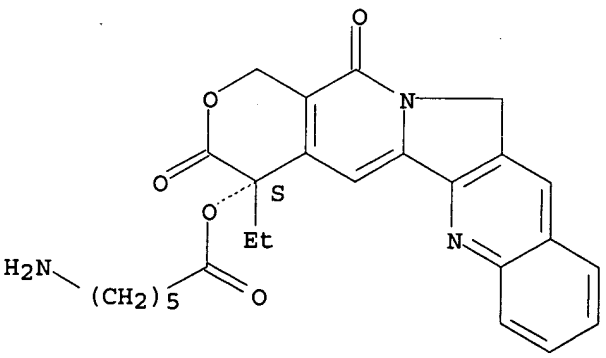
CM 3

CRN 21442-01-3
CMF C7 H13 N O2



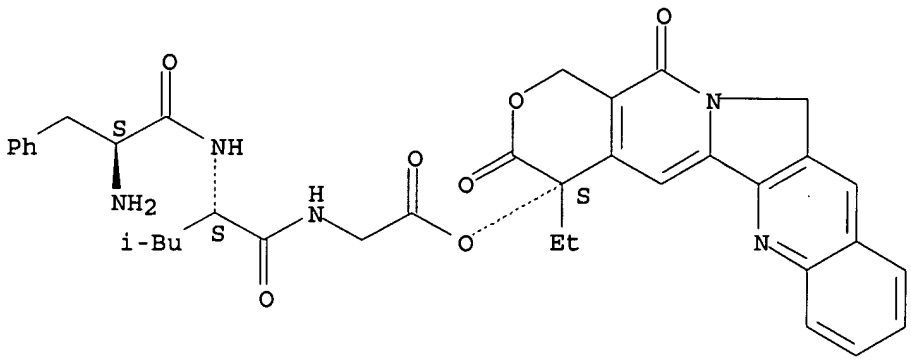
IT **164725-96-6P 164725-97-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of antitumor camptothecin polymer conjugates)
RN 164725-96-6 CAPLUS
CN Hexanoic acid, 6-amino-, 4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 164725-97-7 CAPLUS
CN Glycine, L-phenylalanyl-L-leucyl-, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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L3 1148 S L1 FULL

FILE 'CAPLUS' ENTERED AT 12:08:12 ON 03 NOV 2005
L4 164 S L3

FILE 'REGISTRY' ENTERED AT 12:10:31 ON 03 NOV 2005
L5 STRUCTURE UPLOADED
L6 38 S L5
L7 779 S L5 FULL

FILE 'CAPLUS' ENTERED AT 12:18:09 ON 03 NOV 2005
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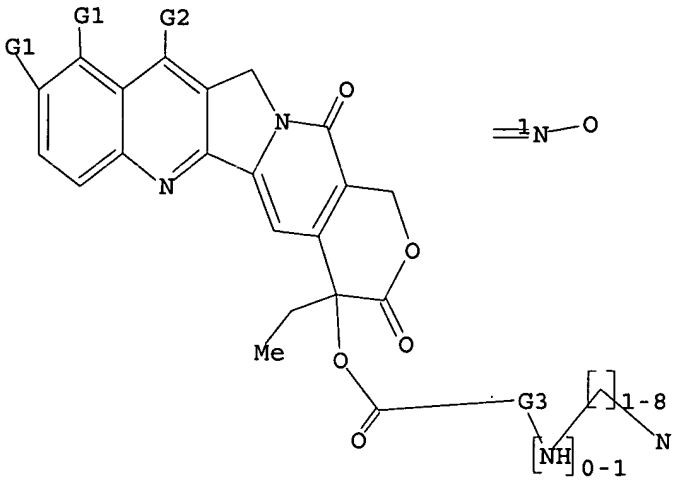
L5 STR




G1 H,OH,MeO,EtO,n-PrO,i-PrO,n-BuO,i-BuO,s-BuO,t-BuO

G2 H,[@1]

G3 Cb,Ak

Structure attributes must be viewed using STN Express query preparation.

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